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**Title of Initiative:** Mechanisms and Interventions to Address HIV-Related Comorbidities in Populations Who Experience Health Disparities

**Authors:** Deborah E. Linares, Ph.D., M.A.; Olga Herren, Ph.D.; Phuong-Tu Le; Seema Desai, Ph.D.; Rina Das, Ph.D.

**Reviewers:** Lisa Barnes, PhD and Mario Sims, PhD

**Objective:** This initiative will support research to examine mechanisms and interventions to address HIV-associated comorbidities among populations experiencing health disparities.

**Background:** It is well established that HIV disproportionately impacts U.S. racial, ethnic, and sexual and gender minority groups. A growing number of people living with HIV (PLWH) in the U.S. are living longer due to the success of antiretroviral therapies. Improving the healthspan—i.e., increasing healthy years in PLWH and reducing barriers to HIV care, such as stigma, that disproportionately impact minority populations—will be critical in improving health outcomes as this population ages.

Although PLWH are living longer, their risk for chronic comorbidities and coinfections increases. Compared to their seronegative counterparts, comorbidities may be acquired earlier in life, which can complicate and accelerate the HIV disease process, manifesting as frailty, organ and functional impairment, and increasing risk of hospitalization and death. PLWH are also at greater risk for HIV-associated non-AIDS comorbidities, such as diabetes; cardiovascular, renal, bone and liver diseases; cognitive impairments; psychiatric conditions; and cancers. These risks and rates of mortality are even greater among populations experiencing health disparities, including racial and ethnic minority groups, sexual and gender minority (SGM) persons, individuals with low socioeconomic status (SES), or people from underserved rural areas. PLWH who are affected by health disparities commonly experience elevated levels of stress leading to greater psychological distress, psychiatric disorders, and other negative health outcomes. As this population ages they also experience a higher burden of disease likely due to multiple factors such as chronic inflammation, immune senescence, microbial translocation, and changes in the gut microbiome and metabolome, possibly leading to accelerated and/or accentuated aging. The combined adverse effects of living with HIV and multimorbidity adversely affects quality of life (QoL), well-being, mental and physical health, as well as SES, with more severe consequences among PLWH who experience health disparities.

Additionally, PLWH who are affected by health disparities often encounter barriers to care due to multiple stigmas related to experiencing intersecting identities that are marginalized (e.g., a Black man identifying as bisexual living with HIV). Social determinants of health (SDOH) such as poverty and access to affordable housing further compound these barriers across the lifespan. HIV-related stigma disproportionately impacts SGM PLWH. Stigma is pervasive across settings

(e.g., clinic, community, workplace), and can inhibit quality of life and physical and mental health by limiting resources through its impact on social networks and help-seeking behaviors. Caregivers of this population may experience exacerbated strain given the multiple stigmas, stressors, and multimorbidity risks this population faces. Given this population's unique challenges, multidisciplinary approaches and further understanding of the multilevel and multidomain mechanisms are needed to understand the burden of comorbidity and increase the healthspan among PLWH who experience health disparities, especially among those who have intersecting identities that are marginalized.

PLWH with comorbidities who are affected by health disparities experienced a disproportionate risk of hospitalization and mortality from COVID-19 infection. The pandemic economically impacted this population substantially and led to increased psychosocial strain and mental illness as well as limited or delayed access to health care, treatment, and testing. However, limited data exists about the extent to which the COVID-19 has exacerbated comorbidity-related disparities among PLWH. Identifying and analyzing the multilevel underlying mechanisms, such as stigma, region, or the effects of social, economic, behavioral, and clinical determinants on comorbidities and QoL among PLWH who experience health disparities, is imperative to develop key points for intervention.

One approach to bolster QoL and improve the healthspan for this population is through successful aging—experiencing satisfaction and well-being as one transitions through the advanced stages of life. Resilience, the ability to adapt while experiencing challenges, is a key aspect of successful aging, which may be associated with protection against stress. Successful aging interventions may support and benefit diverse PLWH as they age and cope with unmet physical and psychosocial needs, as well as buffer the effects of stressors. Comprehensive integrated interventions of successful aging that promote physical, psychosocial, and mental well-being could improve health outcomes and reduce comorbidities among PLWH who experience health disparities.

Limited extant research exists on the mechanisms and pathways of comorbidities among PLWH who experience health disparities, especially related to COVID-19. Although extensive literature exists, little is known about their underlying mechanisms. Furthermore, there are few successful aging interventions seeking to improve the healthspan and QoL among PLWH who experience health disparities. NIH has supported extensive health disparities research on HIV (globally and in the U.S.) and on the prevalence of comorbidities, yet very few studies have focused on the mechanisms of comorbidities, and interventions to increase QoL and promote successful aging among PLWH who experience health disparities. A recent NIMHD grant portfolio analysis (covering fiscal years 2017-2022) identified few funded studies on the comorbid burden, mechanisms of accelerated/acceluated aging due to HIV and comorbid conditions, and strategies to reduce stigma and strengthen social networks; and no funded interventions to promote successful aging and QoL among PLWH with comorbidities who experience health disparities.

**Description of the Initiative:** This current initiative will support multilevel and multidisciplinary projects examining mechanisms and pathways of comorbidities and interventions to promote successful aging and QoL among PLWH who experience health disparities. Research topics may include but are not limited to the following, among the aforementioned populations:

- Identify the comorbid burden among racial and ethnic groups with HIV on QoL
- Examine the interplay of multilevel (e.g., individual, family) factors and how comorbidities may influence HIV disease outcomes in different geographic areas, especially the Southeast and Northeast
- Examine various SDOH such as discrimination and structural racism at neighborhood levels on health among PLWH with multiple identities that are marginalized
- Characterize differences among racial and ethnic groups in biobehavioral mechanisms among individuals with HIV and COVID-19 infection
- Explore behavioral change/lifestyle interventions for modifiable factors such as smoking cessation and mindfulness meditation
- Use peer-based integrated interventions to promote successful aging in multiple settings, drawing on family and intergenerational approaches
- Employ artificial intelligence/machine learning methods to examine the impact of COVID-19 and HIV on health outcomes
- Develop and test novel, multilevel interventions to bolster social support, reduce stigma, promote resilience, and improve health outcomes
- Examine peer-based integrated interventions to promote successful aging in community, clinical, and workplace settings
- Develop and test interventions among SGM PLWH with intersecting identities and multiple comorbidities to improve health outcomes
- Identify the role of health care access and uptake of services in treatment outcomes among PLWH with multiple comorbidities who experience health disparities, and develop interventions to address these disparities
- Develop structural and systems level interventions to coordinate and improve care among patients with comorbidities
- Develop interventions to coordinate and improve health care services among PLWH with multiple comorbidities in rural settings